

### **REMARKS**

Claims 1-16 and new Claims 27-32 remain in the application for further prosecution. Claims 17-26 were withdrawn from consideration as the result of an election of Claims 1-16 without traverse. Accordingly, Claims 17-26 have been cancelled above and may become the subject of a subsequent divisional application. New Claims 27-32 have been added. The new claims are directed to the embodiment of the invention shown in Figs. 3 and 4 and discussed in Example 4.

Claims 1, 5-9 and 13-16 were rejected under 35 U.S.C. 103(a) as unpatentable (i.e. obvious) over Columbus (U.S. 4,233,029) in view of Przybylowicz et al (U.S. 3,992,158). Both references could be relevant to the present invention only by giving Claims 1 and 9 a very broad reading.

The Applicant's invention relates to the problem of distributing liquid samples over reagents disposed on substrates, which are positioned in wells of microfluidic devices. As discussed in paragraphs 0040-0044 of the published application U.S. 2004/0265171 A1 (or page 9, line 20 to page 11, line 19), it is important that the sample is uniformly distributed over the reagents if accurate results are to be obtained. In many cases, the substrates act as capillaries and draw the sample into the substrate. Another problem related to distributing the sample liquid over the reagents is the interference of air bubbles that are not purged from the microfluidic well. Again, the use of microstructures such as those described in the published application at paragraphs 0046-0049 (or page 11, line 21 to page 12, line 25) have been found to assist in uniformly distributing the liquid sample over the reagents immobilized on substrates and in purging air from the microfluidic well. A preferred embodiment described in Figs. 3 and 4 is the subject of new Claims 27-32.

Turning to Columbus, it is evident from his Fig. 1 that if a liquid sample enters opening 26 that the liquid will flow in all four possible directions. Columbus describes movement of liquid along the grooves 44 and the jumping of liquid over the peaks of the grooves until, depending on the amount of liquid present, the entire device 10 is filled. It appears that Columbus intended to provide controlled distribution of the liquid at a uniform rate along all the edges (see column 10, lines 1-6). In a preferred use, the liquid leaves the device and proceeds to a test site where it contacts an electrode (see column 10, lines 7-10, Figs. 9-11). Various types of downstream processing were suggested, see column 9, lines 50-68, but the uniform distribution of the liquid over reagents immobilized on substrates in microfluidic wells was not disclosed or suggested.

As the Examiner noted, it was suggested that reagents could be disposed on the grooved surfaces, but there is no suggestion that the reagents are immobilized on substrates, as in the Applicant's invention. The reference in Columbus to U.S. 3,992,158, cited also by the Examiner, is unclear since the '158 patent concerns multilayer analytical device that features an "isotropically porous spreading layer comprising a non-fibrous material" (Claim 1) that is intended to provide a uniform concentration of the sample to the reagent layer (column 3, lines 30-33). Such a spreading layer should not be equated with the microstructures of the present application. At column 14, beginning at line 34, a typical application of the '158 multilayer device is described. It is obvious that the multi-layer device of the "158 patent is intended for use in an instrument that detects the results of contact of a sample with the reagents. The use of such multi-layered element on the surfaces of Columbus does not correspond to the Applicant's use of microstructures to assure that a liquid sample is uniformly distributed over reagents. Applying the multi-layers of the '158 patent would rely on the "porous spreading layer", rather

than the microstructures described in the present application. In any event, the opposing surfaces of Columbus would not define a fixed volume, such as is inherently the case in the reagent well of a microfluidic chip.

Regarding Claim 5, the Examiner considers the grooved surface 18 to be a substrate. However, in the context of the present invention a “substrate” is a solid material on which the reagent or conditioning agent has been deposited (paragraph 0046 or page 11, line 30 to page 12, line 2). Typically, such substrates are fibrous pads. Thus, the substrates of the Applicant’s application are applied to a well in a microfluidic device. The surface of the well itself is not the substrate. As mentioned above, it is the nature of the substrates that makes it necessary to provide microstructures to assure uniform sample distribution.

Regarding Claim 6, the Examiner again relates grooves 18 of the Columbus device with the Applicant’s substrate. Again, as explained above, Columbus’s grooves 18 are not the Applicant’s substrate.

Regarding Claim 7, the Examiner relates the truncated ridges 46 of Columbus (Fig. 7a) to a ramp. Since a “ramp” is typically defined as an inclined surface, relating the flat ends of a series of grooves to a ramp is not a reasonable interpretation of Columbus.

Regarding Claims 9 and 13-16, the Examiner contends that Columbus teaches all of the Applicant’s apparatus structure. However, it should be evident to one skilled in the art that the Columbus device of Fig. 1 and the Applicant’s microfluidic devices, shown generally in Figs. 1 and 2 and more specifically the introduction of a liquid sample into the well of a microfluidic device in Figs. 3 and 4, are clearly not alike, nor would they function in the same way. Reconsideration is requested.

Claims 2-4 and 10-12 were rejected under 35 U.S.C. 103(a) as unpatentable over Columbus in view of Przybylowicz et al '158 and further in view of Peters (U.S. 6,296,126 B1). The deficiencies of Columbus and Przybylowicz have been discussed above. Peters is a co-inventor in the present application and his patent was cited in paragraph 0014 of the published application. (or page 4, lines 2-5). If, as the Applicant's contend, independent Claims 1 and 9 are patentable, then Claims 2-4 and 10-12 should also be patentable. Although Peters does show posts having wedge-shaped cutouts, he does not suggest the use which the present invention discloses.

Peters was concerned with emptying capillaries into a collecting chamber (see Claim 1). Even in the embodiment of Figs. 7-8, where a row of posts are used, their function is to remove liquid from membrane 32, which then flows via wedge-shaped cutouts to second chamber 27 and then into the third chamber 29. Thus, there is no use of posts to distribute a liquid sample uniformly over reagents on a substrate. Therefore, even if Columbus and Przybylowicz are assumed to make independent Claims 1 and 9 obvious, Peters is not sufficient to make Claims 2-4 and 10-12 obvious and unpatentable.

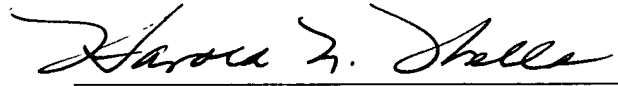
The remaining prior art cited by the Examiner is of interest, but not directly pertinent to the presently claimed invention.

The Examiner is urged to reconsider and withdraw his rejections. If further amendment is considered necessary, the Examiner is invited to contact the Applicant's attorney at the telephone number provided below.

The Commissioner is hereby authorized to charge deposit Account No. 10-0447 (55197-00010USPT) for any fees inadvertently omitted which may be necessary now or during the pendency of this application, except for the issue fee.

Respectfully submitted,

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Date



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